

Urinary Tract Infections in Patients Admitted to the Nephrology Department

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Abstract: Urinary infections (UI) remain among the most frequent problems faced by the clinician and occupy a prominent place in nephrological pathology due to their frequency and severity. The aim of this work is to study the aspect of UI in the nephrology service. *Materials and methods:* This is a prospective study over a period of 5 months (July 2016 – December 2016). *Results:* 115 patients had benefited from cytobacteriological urine exam. The prevalence of UI was 31%. The mean age of patients was 38 years with a female predominance. Renal failure was found in 33% of patients followed by nephrotic syndrome (25%) and kidney transplant (11%). Chronic renal insufficiency was found in 25% of patients and 23% received an Endoxanbolus. The most incriminated species were *Enterobacteriaceae* (81%) with the predominance of *E. coli* (44%) followed by *Klebsiella pneumoniae* (31%) *Enterobacter cloacae* (3%) resistance to C3G by production of Betalactamases with extended spectrum was found in 24% of *Enterobacteriaceae*. Resistance to amoxicillin-clavulanic acid was 72%, fluoroquinolones (34%) and gentamicin (14%). The first-line antibiotic was Ciprofloxacin (62%) and a third generation cephalosporin in 28% of cases. *Conclusion:* Area soned use of antibiotic is necessary in order to prevent the extension of bacterial resistance.

Keywords: Urinary Infection, Kidney Failure, *Enterobacteriaceae*, Antibiotic Resistance, *E. coli*, Ciprofloxacin

1. Introduction

Urinary tract infections are a real public health problem. The increasing antibiotic resistance of the bacteria involved in UI limits the choice of antibiotics and warrants surveillance.

The annual incidence of urinary tract infections is estimated in the United States at 11 million cases and in France at 4-6 million cases [1, 2]. In Morocco, urinary tract infections remain frequent and rank first in hospitals. In nephrology, urinary tract infection is a frequent reason for consultation and is present in a large number of hospitalized patients [3]. Very few studies are available on this topic. Urinary tract infection in patients with renal insufficiency is a complicated urinary tract infection requiring special diagnostic and therapeutic management [4, 5]. It is a frequent

but serious pathology because grafted of a heavy morbidity [6]. The bacteriological samples are precious, indispensable and allow to establish a suitable treatment.

These urinary infections, at the origin of many prescriptions of antibiotics, participate in the pressure of selection of bacterial resistance to antibiotics. As such, we undertook this work whose objective is to study the epidemiological, clinical, bacteriological and therapeutic profile of the urinary tract infection in hospitalized patients in the nephrology department of Mohamed VI University Hospital of Marrakech.

2. Materials and Methods

This is a prospective observational and descriptive study over a 5-month period from July 2016 to December 2016 and

includes all the ECBUs systematically performed on all patients hospitalized in the nephrology department and treated at the laboratory level. Microbiology of Mohammed VI University Hospital of Marrakech.

The data were collected from the medical records of hospitalized patients in the nephrology department and from the database of the microbiology laboratory of the Mohamed VI University Hospital. These data were entered on a record that included anamnestic, clinical, bacteriological and therapeutic variables.

The positive diagnosis of urinary infection was established on the data of the cytobacteriological examination of the urine. Each urinary specimen sent to the laboratory was subjected to a cytobacteriological urinalysis including:

- (1) uroculture with enumeration of bacteria (bacteriuria);
- (2) a microscopic examination to assess leukocyturia and other elements of the urine (red blood cells, crystals, yeasts, etc.).

Included in this study were urinary specimens meeting IU criteria with leukocyturia greater than 104/ ml and a bacterial mono culture considered significant. The threshold of bacteriuria was interpreted according to bacterial species, sex and clinical context. The bacteriuria thresholds of 103 CFU/ml were retained for urinary *E. coli* infections and a threshold of 104 CFU/ ml was retained for Enterobacteriaceae more commonly involved in the setting of nosocomial urinary infections. The identification of bacteria was made on conventional morphological, cultural and biochemical characters. The study of antibiotic susceptibility was carried out according to the technique of diffusion of disks in agar medium and the interpretation was made according to the standards of the Committee of the antibiogram of the French Society of Microbiology (CA-SFM). broad-spectrum beta-lactamase (ESBL) producers were systematically detected by the synergy test between a central disk of amoxicillin + clavulanic acid and beta-lactam disks (cefotaxime, ceftazidime, cefepime and aztreonam). The presence of ESBL was noted in front of a "champagne cork" appearance.

3. Results

During the study period, 115 patients received ECBU. The prevalence of urinary tract infection was 31%. 15% had significant leucocytury with a polymicrobial culture. The median age was 38 years old. 55.6% were female. Renal failure was found in 33% of patients followed by nephrotic syndrome (25%) and renal transplant recipients (11%). Chronic renal failure was found in 25% of patients and 23% benefited from an Endoxan bolus. Figure 1 shows the distribution of IUs documented by reason of hospitalization.

Clinical signs indicative of UTI were very polymorphic dominated by micturition (18.3%) followed by fever (14%) and lumbar pain (10%). The most common clinical forms were asymptomatic bacteriuria (46.7%), cystitis (30.6%) and acute pyelonephritis (PNA).

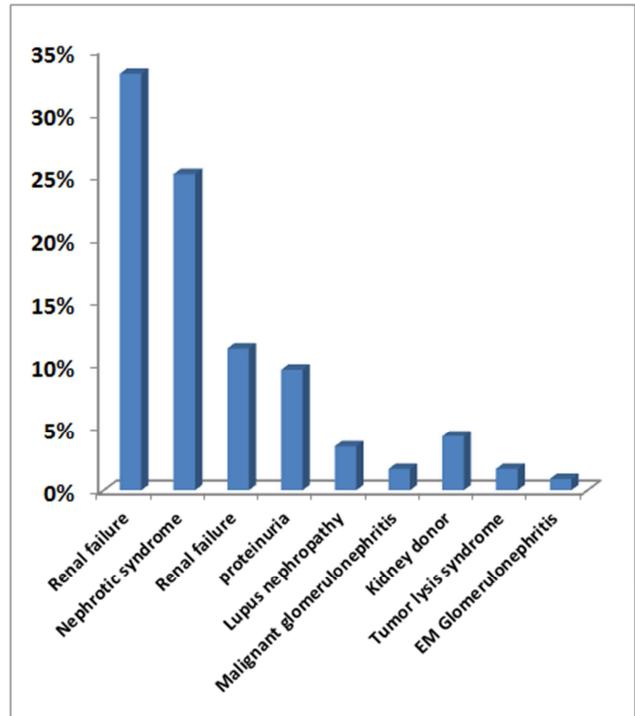


Figure 1. Distribution of IUs documented by reason of hospitalization in nephrology.

The appearance of ECBU was clear in 41% of cases, trouble in (29%) and slightly troublein (22%). Hematuria was present in 81% and leukocyturia in 65% of cases. For completed ECBUs, 31% met the infection criteria positifs, 28% had no criteria for urinary tract infection, germ-free leukocyturia in culture was found in 26% of cases and 15% were polymicrobial. Figure 2 shows the distribution of ECBUs produced during this period according to crop results.

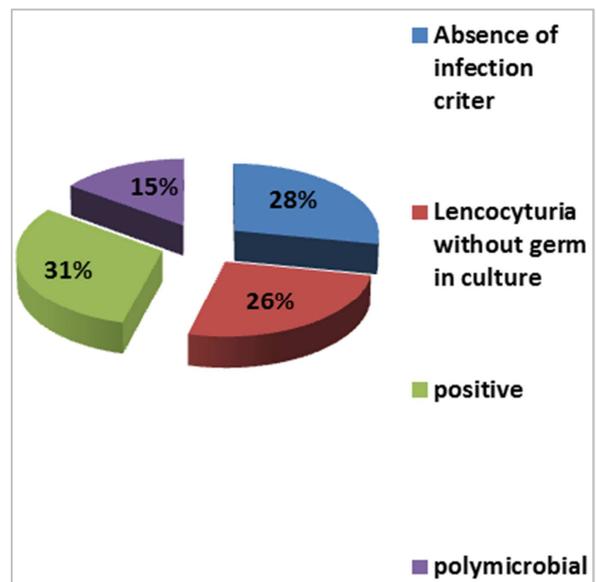


Figure 2. Distribution of ECBUs in Nephrology Patients by Cultures Results.

The most incriminated species were enterobacteria (81%) with the predominance of *Escherichia coli* (44%) followed by *Klebsiella pneumoniae* (31%) and *Enterobacter cloacae* (3%). The resistance of enterobacteria to amoxicillin-clavulanic acid was 83%.

Table 1. Percentage of resistance to antibiotics of uropathogenic enterobacteria (n =29).

Antibiotics tested	Percentage of resistance
Amoxicilline	83%
Amoxicilline+Acide clavulanique	72%
C3G	24%
Ciprofloxacine	34%
Cotrimoxazole	67%
Gentamicine	14%
Amikacine	3%

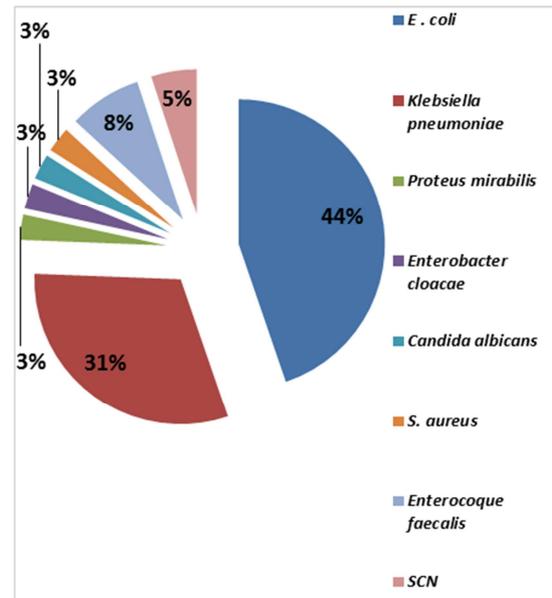


Figure 3. Distribution of uropathogenic bacteria in hospitalized nephrology patients (n = 115).

Table 2. Percentage of antibiotic resistance of the enterobacteriaceae isolated in IU in Nephrology.

Enterobacteriaceae	AMX	AMC	IMP	C3G	CIPRO	SXT	GENTA	AMIKA
<i>E. coli</i>	69%	63%	6%	19%	44%	63%	6%	6%
<i>K. pneumoniae</i>	100%	82%	18%	36%	27%	78%	27%	0%
<i>E. cloacae</i>	100%	100%	0%	0%	0%	0%	0%	0%
<i>Proteus mirabilis</i>	100%	100%	0%	0%	0%	100%	0%	0%

AMX: amoxicillin; AMC: amoxicillin-clavulanic acid; C3G: 3rd generation cephalosporin; CIPRO: ciprofloxacin; SXT: sulfamethoxazole-trimethoprim; GENTA: gentamicin; AMIKA: amikacin; IMP: imipenem.

Resistance to C3G by ESBL production was found in 24% of isolated enterobacteria. Among the uropathogenic Enterobacteriaceae in nephrology, the carbapenem-reduced susceptibility strains represented 10% mainly affecting *Klebsiella pneumoniae* and *Enterobacter cloacae*. Figure 3 illustrates the distribution of uropathogenic bacteria in hospitalized patients in the nephrology department.

Resistance to fluoroquinolones was found in 34% of isolates and gentamicin in 14%. Table I reports the antibiotic resistance rate of the main isolated enterobacteria.

The antibiotic prescribed as first-line was ciprofloxacin in 62% cases and a third generation cephalosporin in 28% of cases.

The evolution was favorable in 90% of the cases. 6% had sepsis and one death was recorded in 4% of patients.

4. Discussion

The urinary tract infection has been the subject of numerous studies because of its frequency and etiological and evolutionary seriousness, motivating prescriptions of antibiotics most often its profile vis-à-vis antibiotics [7]. In this context, the urinary tract infection has often been without bacteriological documentation immediately complicated and requires an early diagnosis and accurate and appropriate care. It can lead to general complications, such as urinary

bacteremia [8].

Most epidemiological studies [9-10] have shown that urinary tract infection is more common in women than in men. In this study, a female predominance was found with a sex ratio H/ F of 0.8 due to anatomical and physiological peculiarities in women.

The average age of 38 years is similar to that reported by a retrospective study that included 145 cases collected in the nephrology department of Ibn Rochd University Hospital in Casablanca (35 years) [3].

This study showed that the prevalence of urinary nephrology infection was high. It was of the order of 31% as demonstrated by many studies [3, 18].

The location of UI in nephrology patients was unique, with 1 in 4 patients in CKD receiving immunosuppression. 20% of the patients were hypertensive and 6% were diabetic. In Casablanca, Bourquia et al. [3] reported 6.2% of diabetes; 1.37% of corticosteroids in the IU of the patient in Nephrology.

The frequency of CKD in this study was similar to that found by CHEMLAL et al. [18] (25%) and lower than TRAORE et al. [17] (49%); this is explained by the ever-increasing frequency of CKD causes, namely hypertension and diabetes in the general population.

Diabetes is a factor favoring urinary tract infection. The frequency of diabetes in this study is close to that found by

TRAORE *et al.* [17] (10%) and low compared to CHEMLAL *et al.* [18] (35.4%).

Burnout (18.3%), fever (14%), lumbar pain (10%) and dysuria (9%) were the main manifestations of symptomatic urinary tract infection. In Bamako TRAORE *et al.* [17] found 58.7% of vomiting, 46.7% of fever, 15.8% of lumbar pain and 11.9% of micturition.

In Casablanca Bourquia *et al.* [3] report a prevalence of micturition (57%) and lumbar pain (41%). The frequency of micturition and lumbar pain in this study were close to those found by TRAORE *et al.* And too low compared to the casablanca study.

Leukocyturia may be absent in 20 to 40% of cases [20]. Isolated bacteriuria that reaches significant values should always point to a urinary tract infection. Indeed, although there are quite close correlations between bacteriuria and leukocyturia, discrepancies between these two data can be seen especially in diabetic subjects and in pregnant women.

Microscopically, leukocyturia was present in 75 cases (65%), microscopic hematuria in 81% and bacteriuria (52%).

According to a national study, the authors report 80-90% leukocyturia, 45% hematuria and 72.41% bacteriuria [3].

The nature of the isolated germs varies according to the studies. In a prospective study started from (2012 to 2014) conducted at the Nephrology Department at the Oujda Regional Hospital, the isolated germ was an *E. coli* in 58.3% and *Klebsiella* in 29.2%. *Candida albicans* was associated in 4.2% of cases. 16.7% of the bacteria were resistant to C3G by ESBL production [18]. According to another study conducted in the nephrology department of CHU ibn Rochd, the most frequently found organisms were enterobacteria in 61% of cases, with the predominance of *E. Coli* (28%), followed by *Klebsiella* (17%) and *Proteus* (6%) [3].

Moreover, in this series, enterobacteria dominated the profile of uropathogenic germs with the predominance of *E. Coli* followed by *Klebsiella pneumoniae* and *Enterobacter cloacae* which joins the epidemiology of urinary tract infection in children and adults in the literature.

The study of the susceptibility of enterobacteria to antibiotics revealed an increase in the level of resistance for

the majority of the antibiotics tested. This finding, reported also by various studies in particular, a prospective study at the Oujda hospital. Indeed, the authors included in this study all patients hospitalized in the nephrology department, with renal impairment defined by a glomerular filtration rate <60 ml/ min/ m² and/ or chronic hemodialysis and presenting a documented urinary tract infection. Isolated enterobacteria were resistant to amoxicillin-clavulanic acid in 83% of cases, cephalosporin of third generation in 25.5% and quinolones in 29.8% [18].

This increase in the resistance found and the consequence of the pressure of selection due to the massive prescription and the often abusive use of the antibiotics with broad spectral as well in hospital environment as in community, as well as cross-transmission of acquired resistances with plasmid determinism. The resistance of *E. Coli vis-à-vis* the majority of ATB has increased in a way progressive.

This increase was more marked for laiprofloxacin (44%) and the sulfamethoxazole + trimethoprim combination (63%). This is close to the European data which showed that the sensitivity of *E. coli* antibiotic has declined steadily over the last decade in many countries [19]. This surveillance confirms the worrying nature of the evolution of *E. coli* resistance. *E. coli* with fluoroquinolones.

This study showed high but relatively stable resistance levels for amoxicillin, amoxicillin-clavulanic acid, and sulfamethoxazole + trimethoprim. This is probably due to a large prescription by our doctors strongly limiting their interest in probabilistic treatment of UI. These results are consistent with other Tunisian [30] and European studies [23].

In this study, resistance to C3G by ESBL production was found in 24% of isolated enterobacteria, close to literature data. The problem related to the production of an ESBL is especially the frequent presence of co-resistances making the multi-resistant strains with great power of dissemination.

In this study, amikacin remains the most active molecule, which is consistent with results found in New Zealand [21]. FQ and the combination sulfamethoxazole + trimethoprim were the molecules most affected by resistance.

Table 3. Comparison of the percentages of resistance of *E. coli* Antibiotic according to studies in nephrology patients.

Study	Ampicilline	Céphalosporin 3rd génération	Ciprofloxacine
Our series (16)	69	19	44
Oujda(28)	75	17.85	28.57
Tunisie (20)	68	6.2	9
Turquie (25)	73.3	-	12
USA (26)	39.3	-	6.8
Russie (27)	37.1	-	4.5
Canada (26)	33	-	1.1

As a result, the frequent use of carbapenems to treat C3G-resistant enterobacterial infections has led to the emergence of carbapenemase-producing enterobacteria with the risk of therapeutic impasse and with all the ecological and infectious consequences that this may have.

The emergence of multi-resistant urinary germs is a big problem in everyday practice. It is at the origin of the

prolongation of the duration of hospitalization and consequently of a morbidity more important. The emergence of resistance is intimately linked to previous contact with antibiotics, hospitalizations, prolonged antibiotic therapy, sometimes unjustified, and abusive antibiotic prophylaxis. The fight against this phenomenon requires compliance with rules of antibiotic prescription, respect for asymptomatic

bacteriuria and the implementation of a policy of antibiotic therapy [13-14].

Antibiotic susceptibility of incriminated organisms, especially Enterobacteriaceae, is declining steadily throughout the world, but with differences between series. We compared our data with the literature to look for a difference between regions. Table III reports the resistance of *E. coli*. antibiotic coli according to different studies) [15, 16]. Differences in sensitivity are due to selection pressure due to the frequent use of antibiotics. The clinic and the simple biological examinations are often sufficient for the diagnosis of localization. In this series, cystitis is dominated profile (31%) and pyelonephritis in 22.5% of cases. These percentages are also found in a study conducted in the nephrology department of CHU ibn Rochd [3], where the isolated IU was found in 45% of cases, cystitis (25%) and Pyelonephritis (20%). with a predominance for the young adult. The female sex was the most affected. Cystitis was the most observed clinical form.

The epidemiology of uropathogenic germs did not show any particularities in the patient in nephrology. The problem of resistance was posed in enterobacteria with 24% C3G resistance and 10% carbapenem-reduced susceptibility strains in ESBL-producing strains of *Klebsiella pneumoniae* and *Enterobacter cloacae*. Faced with this increase in the frequency of antibiotic resistance in uropathogenic enterobacteria, the hospital should take a number of steps to prevent the spread of multidrug-resistant enterobacteria. This prevention requires the strengthening of hospital hygiene measures, the rational prescription of antibiotics guided by the results of the antibiogram, the screening and the technical and geographical isolation of patients with multidrug-resistant bacteria.

5. Conclusion

Urinary tract infection is the most common bacterial infectious pathology in the general population, including in patients with renal insufficiency. The main issue in patients with renal insufficiency is the adaptation of the dosages of antibiotic treatments. The best treatment is prevention by early detection of urinary tract infections and adherence to good antibiotic prescribing practices. Controlling bacterial resistance to antibiotics is a public health priority that requires concerted action in health and research institutions. Prevention of cross-transmission and reduction of selection pressure by rational use of antibiotics are two essential components.

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